FF183(revised). Further, Janssen's own prior art compound Setoperone did not have any anticholinergic properties. *Tr. 292, ll. 20 to 293, l. 7 (M); DTX-142* (Setoperone has no anticholinergic activity)*; DTX-143.*

4. Even if One Assumes That the Anticholinergic Theory Was the "Dominant" Theory, it Does Not Follow That Obviousness Cannot be Established Unless This Theory is Followed

Janssen's own witnesses admitted that the existence of the so-called anticholinergic theory would not have stopped one skilled in the art from pursuing an antipsychotic compound under the combined dopamine and serotonin theory. Indeed, Janssen's Dr. Meltzer conceded that the dopamine/serotonin theory was viable and accepted by those skilled in the art in the early 1980s, and that one skilled in the art *would have been motivated* to develop a compound in accordance with this theory, *i.e.*, a compound having both dopamine and serotonin antagonism, such as Pirenperone. *See DFF176.* Under these circumstances, Defendants' *prima facie* case remains unscathed.

Dr. Meltzer's admission is consistent with Federal Circuit authority which has expressly rejected Janssen's argument to the contrary—that an obviousness case must be based on the preferred or most desirable combination or theory. In a recent case, the Federal Circuit stated:

> [t]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination, not whether

> there is something in the prior art as a whole to suggest that the combination **is the most desirable combination available**.

In re Fulton, 391 F.3d 1195, 1200 (Fed. Cir. 2004) (emphasis added). Indeed, in *In re Gurley*, the Federal Circuit found claims to one of two alternative resins obvious, even though the prior art reference described the claimed resin as usable, but inferior. *See In re Gurley*, 27 F.3d 551, 552-53 (Fed. Cir. 1994). The combined dopamine and serotonin theory, like the claimed resin in *Gurley* which was supported by prior art teaching, provides more than adequate motivation to one skilled in the art. *See DCL64 and DCL65.*

Certainly, Pirenperone was a far superior candidate relative to those championed by Janssen—clozapine and haloperidol—the former suffering from a serious side effect (i.e., it killed people) whose origin was unknown (as compared to the known source of Pirenperone's short half-life), while the latter was known to be converted into an inactive metabolite in the body. *See, e.g.,DFF194-DFF195 (clozapine caused deaths in humans) and DFF131.*

The foregoing provides support for the following additional conclusions of law:

DCL64. The Federal Circuit has expressly rejected an approach that an obviousness case must be based on the preferred or most desirable combination or theory. Instead, the question should be whether there is something in the prior art to suggest the desirability of making the combination:

> [t]he question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination, *not whether there is something in the prior art as a whole to suggest that the combination is the most desirable combination available.*

In re Fulton, 391 F.3d 1195, 1200 (Fed. Cir. 2004) (emphasis added).

DCL65. An obvious composition does not become patentable simply because it has been described as inferior to another product for the same use. For example, the Federal Circuit found claims to one of two alternative resins obvious, even though the prior art reference described the claimed resin as usable, but inferior. *In re Gurley*, 27 F.3d 551, 552-53 (Fed. Cir. 1994).

VI. SECONDARY CONSIDERATIONS

Janssen misstates Defendants position regarding secondary considerations of nonobviousness. Defendants have never suggested that secondary considerations should not be considered by the Court. On the contrary, under *Graham* they must be considered. However, because the secondary considerations are not commensurate in scope with the claims (as they must be), Defendants continue in their assertion that the secondary considerations Janssen raised at trial with respect to Risperidone and only Risperidone are an ineffective rebuttal to their *prima facie* obviousness case. Defendants have addressed this issue in a motion *in limine* entitled "*Motion in Limine to Preclude the Introduction of Evidence by Janssen of*

Alleged Secondary Considerations of Nonobviousness Relating to Risperidone," and incorporate by reference the arguments set forth in that motion.

Realizing Defendants' position on secondary considerations is meritorious, Janssen now desperately attempts to bolster its position with a new argument, *i.e,*. three secondary considerations of nonobviousness attach to Compound 11—long-felt need, failure of others and respect to the patent. This argument is so lacking in merit, it should be dismissed out of hand.

No competitor respects the '663 patent because of its inclusion of Compound 11—Janssen admits that Compound 11 is and has never been a commercial product. *See DFF209.* Indeed, Janssen fails to explain how this non-commercial compound somehow has the "respect" of its competitors, satisfied a long-felt need in the industry, or overcame the "failure of others." The evidence concerning Compound 11 in the record conclusively proves the opposite—Compound 11 never left Janssen's laboratory. *See DFF201-DFF211.*

REDACTED

REDACTED

Janssen continues to contend that the asserted '663 patent claims are in "Markush" format, that Risperidone and Compound 11 are related, and that secondary considerations concerning Risperidone also apply to Compound 11. This, of course, fails to recognize that the compounds are two different species, and are recited in the alternative in the '663 patent claims (*See claims 6, 12 and 18 of DTX-1)*. These issues, in addition to much of the case law relied on by Janssen (*e.g., Applied Materials*), are addressed in Defendants' motion *in limine* on secondary considerations, identified *supra.*

In a last-ditch effort to lend credibility to its argument, Janssen (*JFF/CL ¶ 231*) again resorts to half-truths by mischaracterizing a district court's decision in the *Glaxo v. Teva* case. *See Glaxo Group Ltd. v. Teva Pharms. USA, Inc.*, 2004 WL 1875017 (D. Del. Aug. 20, 2004). Unlike the present case wherein each claim recites at least two distinct chemical species, the court in *Glaxo* clearly indicates that the *asserted* claims were limited to a single compound—ondansetron—and not

to any "genus" or "Markush" group which includes ondansetron (as wrongly asserted by Janssen). *See Glaxo,* 2004 WL 1875017 at *12 & *18 (¶ *80 ("The '789 patent specifically claims a method of treatment . . . an effective amount for the relief of nausea and vomiting [the compound known as ondansetron]", ¶ 87 ("The '628 patent claims a method of treatment . . . of nausea and vomiting of [the compound known as ondansetron].").

The fact that the patents asserted in *Glaxo* may also contain claims directed to a relatively broad chemical genus which includes ondansetron is thus irrelevant; the *Glaxo* court indicates that only those claims specifically limited to the chemical species ondansetron were asserted, and the court's reliance on secondary considerations directed to ondansetron is therefore understandable and proper. The facts in *Glaxo* are clearly distinct from the facts in the present case wherein the claims are directed to at least two distinct chemical species Risperidone and Compound 11.

Janssen also attempts to rely on a second case, *E.I. duPont*, in an attempt to support its commercial success argument. This reliance is misplaced, however, because the nonobviousness determination reached by the district court, along with that court's reliance on commercial success, were subsequently vacated by the Federal Circuit. Accordingly, the district court case is of no help in the present case. *See E.I. duPont de Nemours & Co. v. Phillips Pet. Co.,* 849 F.2d 1430, 1440

(Fed. Cir. 1988) ("[T]he district court's judgment that Phillips did not prove invalidity under 35 U.S.C. § 103 is vacated for all claims . . .")

Even if one accepts the standard set forth in *E.I. duPont*, the facts therein are far different from those present here. In *E.I. duPont*, the evidence showed that licenses to an entire family of patented copolymers were taken by many players in the chemical industry, and that the industry decided to commercialize only a few of the patented copolymers. *Id. at 1369*. In accepting sales of the least–expensive patented copolymers as evidence of commercial success of all patented copolymers, the court cited their lower cost as the basis, and did not discount the properties or performance of the other more expensive copolymers. *Id. at 1371*. This is unlike the present case where Janssen failed to present any evidence of a license of the '663 patent, let alone evidence that all of the compounds claimed in the '663 patent possessed the same activity. Indeed, the unrebutted testimony of Dr. Wolff was that Risperidone had unexpected properties (formed an active metabolite in the body), while Compound 11 (or any of the other claimed compounds) had no such properties. *DFF210-211*. Indeed, the evidence confirmed that Compound 11 never left Janssen's laboratory. *DFF201-209; DFF213-214*.

The foregoing supports the following additional findings of fact:

DFF329. **REDACTED**

REDACTED

DFF330.

VII. INEQUITABLE CONDUCT

Mylan has proven that inequitable conduct occurred in the prosecution of the '663 patent by clear and convincing evidence. *See Section V. of Defendants' FF/CL. See also Fox Indus., Inc. v. Structural Preservation Sys., Inc.*, 922 F. 3d 801, 803 (Fed. Cir. 1991). Janssen, faced with its own, undisputed admissions (1) that Janssen itself knew that Pirenperone was a potent dopamine antagonist (of course it did, as it published prior art to that effect) and (2) that it did not disclose Pirenperone's dopamine activity to the Patent Examiner, *PFF 238* now resorts to

desperate means to overcome an inevitable holding that the '663 patent is not enforceable.[4]

In fact, when Janssen desperately opposed Mylan's Motion to Amend its Answer to add the inequitable conduct defense, Janssen adopted a different argument (abandoned at trial) that Pirenperone's property as a potent dopamine antagonist was not material because such information was cumulative with respect to allegedly similar data relating to another Janssen compound, Setoperone. D.I. No. 56, pp. 12-14[5]. The logic behind the "cumulative in view of Setoperone" theory was so contorted that even Dr. Dellenbaugh, who prosecuted the application, and Janssen's experts, evidently could not articulate it at trial. Indeed, Janssen did not even mention anything being "cumulative" at trial. Now, without trial record support, Janssen resurrects the "cumulative in view of Setoperone" defense to inequitable conduct but, again, the defense is factually and legally wrong.

As expected, after doing everything within its power to stifle any attempt to obtain discovery related to Mylan's inequitable conduct defense, Janssen

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[4] Defendants' "Motion for an Order Directing Entry of Certain Admitted Facts into the "Stipulated Facts" Section of the Pretrial Order or, in the Alternative, Requesting that the Court take Judicial Notice of These Admitted Facts" is currently *sub judice*.

[5] D.I. No." refers to "Docket Index Number," *i.e.,* the number assigned by the Court to papers filed with the Court. D.I. No. 56 is Janssen's letter-brief in opposition to the Mylan's motion to add its inequitable conduct defense/counterclaims of May 16, 2006.

complains that Mylan has failed in its efforts. Janssen now argues that there was no intent to deceive by asserting as facts numerous conclusions that were never established at trial, all of which, of course, can be traced back to Janssen's stonewalling of valid discovery. *See, e.g., JFF/CL ¶¶ 297-303; ¶¶ 315-317; ¶¶ 321-322; ¶¶ 324-326; and ¶ 332.*

A. DR. JANSSEN

Janssen argues that Dr. Janssen had no duty to disclose because he had no relevant involvement in the '663 patent. Specifically, Janssen states that "it is undisputed that Dr. Janssen had no involvement whatsoever in the prosecution of the '663 patent" and that Dr. Janssen's role was simply to request the Janssen patent department to begin preparing applications when the scientific research had reached the appropriate point, citing to the testimony of Dr. Dellenbaugh. *See JFF/CL ¶ 315.* Dr. Dellenbaugh was used in an attempt to further explain (without any foundation whatsoever) that Dr. Janssen played no part in the prosecution of the '663 patent. Janssen is wrong. During cross-examination Dr. Dellenbaugh admitted that as a general business practice, patent applications in the United States were only filed with the approval of Dr. Paul Janssen. *See DFF277.*

B. DR. AWOUTERS

Janssen argues that Dr. Awouters "truthfully submitted a declaration describing the characteristics of a different compound, ketanserin." *See JFF/CL ¶*

280. The exact background of Dr. Awouter's Declaration, however, remains a mystery. *See DFF283.*

Janssen then argues that no evidence exists "to show that Dr. Awouters had any reason to believe that Pirenperone or its dopamine antagonism was important to the prosecution." *See JFF/CL ¶ 280.* Of course any lack of evidence is due to Janssen's improper blocking of discovery by Defendants as to Dr. Awouters as explained by Mylan in its opening post-trial brief. *See, e.g., DFF283, DFF288-DFF292 & DFF293-DFF296; DCL49-52.*

Janssen now relies on the inability of Dr. Awouters to attend trial because he is ill. However, there is no explanation as to how Janssen's attorneys became Dr. Awouter's attorneys, there is no record as to why he refused to testify in a deposition, there is no explanation as to why Janssen's attorneys told Mylan's attorneys not to contact Dr. Awouters, and there is no explanation as to why the only discovery to which Dr. Awouters would submit was discovery under the Hague Convention to which Dr. Awouters country of residence (Belgium) is not a party.

But, what we do know about Dr. Awouter's involvement in the prosecution of the '663 patent is that there is more to the story, as explained in Defendants' opening brief. *See, e.g., Section V.C.4.-5. of Defendants' FF/CL; DFF284-DFF287.* We know that Mr. Kennis discussed the prosecution of the '663 patent with Dr. Awouters. *See DFF286.* As explained in Defendants' opening brief, and

in Mylan's pending motion, the missing witness rule should apply as to Dr. Awouters and inferences as to what he would have testified about at trial should be drawn against Janssen. *See DCL49-DCL52*; "Defendant Mylan Pharmaceuticals, Inc.'s Motion *in Limine* to Preclude Evidence Relating to Dr. Awouters' Actions or State of Mind and for an Interference that His Testimony Would Have Been Unfavorable to Janssen."

C. DR. DELLENBAUGH

Finally, as to Dr. Dellenbaugh, Janssen's arguments once again are as expected. Dr. Dellenbaugh, who in his deposition testified that—as a general practice during the early 1980s—he talked to Janssen inventors by phone or in person regarding the applications he was working on for them (*See DFF254);* he frequently visited Janssen in Belgium *(DFF252-DFF253)*; he kept the Janssen patent department aware of the status of the U.S. prosecution *(DFF250)*; he had been given a compilation of Janssen compounds, their structures and properties, that had been prepared for him by the Janssen patent department *(DFF268)*; he was keenly aware of the importance of dopamine antagonism to the purported invention *(DFF251)*; and he was in charge of the prosecution of the '663 patent application *(DFF248)*, is now to be believed when he testified that he had no knowledge that Pirenperone was a potent dopamine antagonist? Further straining believability, Dr. Dellenbaugh after having been confronted at trial with an IDS from the '663

application which he signed and which states "after consultation with inventors..." *(DFF257)* and testifying (at least at his deposition) that his usual practice was to talk to inventors by phone or in person *(DFF254)*, would have the Court believe that he did not even discuss the '663 application with the inventor, Mr. Kennis *(DFF255)*. Mylan submits otherwise. Dr. Dellenbaugh's self-contradictory testimony and implausible representations of his own ignorance of key facts leaves him with no credibility. Accordingly, the Court simply should not believe Dr. Dellenbaugh's protestations of ignorance and should infer that he knew of Pirenperone's dopamine antagonist activity, knew that this information was material, and that he purposely failed to disclose that information to the USPTO. *See Bayer AG v. Housey Pharm., Inc.,* 385 F. Supp. 2d. 578, 582 (D. Del. 2005), *aff'd nonprecedential,* No. 06-1083 (Fed. Cir., Aug. 4, 2006).

Janssen's argument that Dr. Dellenbaugh's actions demonstrate "good faith" because he disclosed the Setoperone patent demonstrates yet another of Janssen's unfortunate attempts to hide behind half-truths. Indeed, Dr. Dellenbaugh submitted an IDS that identified the Setoperone patent. *See DFF268 citing DTX-172.* Of course, by the time that Dr. Dellenbaugh submitted the IDS on January 31, 1986 *(DTX-172)*, the Examiner had already issued a first Office Action on October 28, 1985 in the '663 parent application, and in that Office Action cited the Setoperone patent *(PX 2)*. The timing alone clearly indicates that there was no voluntary action by Dr. Dellenbaugh in citing the Setoperone patent. Indeed, there

is no showing of good faith at all involved in Janssen's prosecution of the '663 patent. Further, how disclosure of the Setoperone patent (as pointed out, which was cited by the Examiner before Dr. Dellenbaugh even filed an IDS) relates at all to Janssen's failure to disclose Pirenperone's potent dopamine activity to the Patent Examiner remains a mystery. The concepts simply are not related.

Moreover, and once again, Janssen applies the wrong standard for materiality. The question is not whether a reasonable Examiner would have allowed the claims to issue after consideration of the improperly withheld information. *See DCL41; Digital Control Inc. v. Charles Machine Works,* 437 F.3d 1309, 1313-19 (Fed. Cir. 2006); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.,* 326 F.3d 1226, 1237-68 (Fed. Cir. 2003) (withheld reference was material notwithstanding Patent Examiner's determination that it did not render the invention unpatentable); *Merck & Co. v. Danbury Pharmacal, Inc.,* 873 F.2d 1418, 1421-22 (Fed. Cir. 1989) (withheld prior art and information was material even though it did not render the patent claims invalid). The correct inquiry is whether the information that was withheld was "material," *i.e.,* was there a substantial likelihood that a reasonable Patent Examiner would have considered it important in deciding whether to allow the application to issue as a patent. *See DCL40;* 37 C.F.R. § 1.56(a) (1984)); 37 C.F.R. § 1.56(a) (1985); *Dayco Prods., Inc. v. Total Containment, Inc.,* 329 F.3d 1358, 1363-64 (Fed. Cir. 2003); *Digital Control, Inc.,* 437 F.3d at 1313-19. Even if Janssen is correct (while is not correct) in arguing

that the '663 patent would have been granted if the USPTO had known of Pirenperone's dopamine antagonism, that argument remains legally irrelevant.

D. JANSSEN'S ATTEMPT TO DENIGRATE MYLAN'S INEQUITABLE CONDUCT DEFENSE FALLS FLAT BECAUSE OF DELAYS CAUSED BY JANSSEN

Janssen once again attempts to defend against Mylan's charge of inequitable conduct because Mylan was cautious in asserting that defense. Yes, it is true that Mylan waited to raise the defense of inequitable conduct until Mylan was provided the discovery by Janssen to which it was properly entitled. The Court will recall that Janssen improperly withheld production of its NDA and IND from Mylan until it was ordered by this Court to produce them. *See DFF285-DFF287.*

As a result of reviewing the improperly withheld 1.4 million pages or so of documents, Mylan indeed did find only one document of interest—a document which showed that at the same time the Patent Examiner was looking for prior art compounds that had dopamine antagonism and Dr. Awouters was preparing (or having prepared for him) his Declaration for submission to the USPTO, Dr. Awouters and Dr. Janssen were drafting an internal research report that showed on its face not only that Janssen's prior art compound, Ketanserin, had no dopamine antagonism, but that Pirenperone indeed was a potent dopamine antagonist that compared favorably with Risperidone. *See DFF262.*

Janssen dismisses this report as irrelevant and merely an earlier version of a paper later published by Janssen. *See JFF/CL ¶ 257.* Again, this is nothing more than the expected response by Janssen, as it has been repeated so often. In fact, as explained before, that internal report by Drs. Awouters and Janssen is actually much more. The report confirms that at the same time Janssen knowingly submitted to the Patent Examiner the data in the Declaration (by Janssen's Dr. Awouters) establishing Ketanserin's lack of antipsychotic activity. Dr. Awouters and others at Janssen (Dr. Paul Janssen) were writing the Janssen research report which showed the full story. *See DFF262.*

That report, besides showing that Ketanserin was not a good antipsychotic, established that Janssen's prior art compound Pirenperone was actually a better antipsychotic than Risperidone based on Janssen's own predictive animal model test. *See DFF262.* This can be easily seen from the following table which is taken directly from the aforesaid Janssen report:

Compounds	Apomorphine dopamine D_2 antagonism
Ketanserin	0
Pirenperone	++++
Risperidone	+++

See DTX-203, p. JJRP0030606

The "0" shows that Ketanserin had no activity as a dopamine antagonist (i.e., it would be a poor antipsychotic), while Pirenperone was the best (i.e., it would be a good antipsychotic). *See DTX-203, p. JJRP00370606 (legend).* Again, it was Janssen itself who told the Patent Examiner that this test relating to dopamine antagonism was "predictive" of antipsychotic activity, yet Janssen failed to forward this important data regarding Pirenperone to the Patent Examiner for consideration. *See DFF79; DFF87-DFF89.*

Therefore, by Janssen's own criteria for judging the effectiveness of an antipsychotic drug (as set forth in their statements to the Patent Examiner), Dr. Awouters and Dr. Paul Janssen knew that Pirenperone was at least as promising of an antipsychotic as Risperidone, if not better, and was clearly better than Ketanserin. By not telling this to the Patent Examiner, Janssen (including Dr. Awouters and Dr. Paul Janssen) intentionally withheld this highly material information from the Examiner. Dr. Awouters was under a duty to disclose this

information as he was materially involved in the prosecution of the application that led to the '663 patent as he signed the key Declaration. Dr. Janssen was under such a duty as he also actually approved the filing of the applications that lead to the '663 patent.

As a consequence of Janssen not being truthful with the Patent Examiner, the Examiner never used (or even mentioned) Pirenperone. *See PX 2.* Further, and as Janssen well knew, the Patent Examiner had also not been provided with any of the scientific literature available in the early 1980s that disclosed Pirenperone and its activity as a potential antipsychotic drug. *See JFF/CL ¶ 284; DFF244; PX 2.*

Janssen attempts to diminish the significance of the withheld research report by stating (correctly) that Mylan has known for a long time that Janssen was aware that Pirenperone is a dopamine antagonist and did not disclose it to the Patent Examiner. But Mylan previously was lacking a document demonstrating that there was *contemporaneous recognition* at Janssen of the comparative dopamine data relating to (1) the subject matter of the '663 patent (Risperidone), (2) the subject matter of the Examiner's rejections (Ketanserin) and (3) Janssen's highly material prior art compound (Pirenperone), *at the time that the Awouters Declaration was submitted.*

Of course, Mylan was aware that Dr. Paul Janssen and Dr. Awouters published the later paper that contained such comparative data, but Mylan had no way of knowing that the comparative data set forth in that paper existed at the

same time that the Awouters Declaration was prepared and submitted to the Patent Examiner.

As the Court is aware, intent is usually proven by inference from other facts. An overwhelming inference of an intent to deceive the Patent Examiner now exists because it is absolutely clear that Dr. Janssen and Dr. Awouters had the relevant true prior art comparison data in their hands in October 1987 when Dr. Awouters' Declaration was submitted to the Patent Examiner and did not disclose the same. *See DCL42-DCL46.*

Janssen mightily attempts to argue that Mylan should have known that this research report existed in October 1987, because the paper published in September 1988 stated that the final draft was submitted for publication in early February 1988, and since that document was a final draft, there must have been an earlier draft (containing unknown information, of course), and that because there was such an earlier draft it must have existed in October 1987 and that it must have contained the withheld information now relied by Mylan. *See JFF/CL ¶¶ 284-287.* This is nothing more than attorney argument.

VIII. JANSSEN'S NEW ASSERTION THAT DOPAMINE ANTAGONISM IS IRRELEVANT TO THE PROSECUTION OF THE '663 PATENT STRAINS CREDULITY

A. THE PROSECUTION HISTORY MAINTAINS THAT ANIMAL TEST MODELS, *I.E.* THE ATN TEST, ARE PREDICTIVE OF ANTIPSYCHOTIC ACTIVITY

In *JFF/CL ¶ 305*, Janssen is now attempting to confuse the Court by again uttering a half-truth. Indeed, nowhere in the prosecution is there a statement made in *ipsis verbis* that the Patent Examiner was looking for dopamine activity in prior art compounds. Rather, she was looking for evidence of antipsychotic activity. But, how was she to determine whether or not compounds possessed such activity? Not by the use of the word "antipsychotic" *per se* in describing them, as Janssen would now have one believe. No, at the behest of Janssen, the Examiner was sent looking for compounds that were active in animal test models such as those "used for evaluation of the claimed compounds"—*i.e.,* the ATN test which Janssen stated "had been shown to be predictive of efficacy in treatment of a variety of psychotic diseases." *See, e.g., DFF220-DFF228; DTX-176, p. 4.* Janssen further told the Examiner that "*the model itself indicates for which uses the product would be employed.*" *See DTX-176, p. 4* (emphasis added). According to Janssen's own words, if a compound did well in the predictive ATN animal test, it would *de facto* be an antipsychotic.

B. JANSSEN INTERCHANGEABLY USES "APOMORPHINE" ACTIVITY AND "DOPAMINE" ACTIVITY AS EQUIVALENT TO "ANTIPSYCHOTIC" ACTIVITY

So was dopamine activity of a compound important to the examination of the '663 patent? Of course it was, although one must be aware that "apomorphine" activity and "dopamine" activity are used interchangeably by Janssen as surrogates for "antipsychotic" activity. *See, e.g., DFF74.* For example, during prosecution of the '663 patent, Janssen stated that "[a]s shown in the Declaration, the compound ketanserin was ineffective to antagonize *apomorphine-induced agitation* in rats. Accordingly, ketanserin does not possess significant anti-psychotic activity." *See DTX-176, p. 6* (emphasis added). In referring to that prosecution argument in its Letter Brief in Opposition to Mylan's Motion to Amend, Janssen used its alternate phrasing: "In that declaration, Dr. Awouters accurately recited test data related to *dopamine* and serotonin *antagonism* by ketanserin …." *D.I. No. 56, p. 8* (emphasis added). During the trial, Janssen's attorney Mr. Diskant again equated apomorphine antagonism and dopamine antagonism. *See DFF331.*

For Janssen to now claim that the dopamine antagonism of Pirenperone or any other compound "was of no relevance to any possible issue before the Patent Office" (*JFF/CL ¶ 305*) strains credulity.

The foregoing supports the following additional finding of fact:

DFF331. The terms "apomorphine activity," "dopamine activity," and "dopamine antagonism" are used interchangeably by Janssen as surrogates for "antipsychotic activity." *See, e.g., DTX-176, p. 6; D.I. No. 56, p. 8; Tr. 213, l. 23 to 214, l. 1; 215, ll. 8-11.*

C. JANSSEN'S LAST-MINUTE PLEA THAT PIRENPERONE IS NOT AN ANTIPSYCHOTIC

Janssen now argues that Pirenperone is not an antipsychotic. Janssen then argues that the Patent Examiner was not interested in dopamine activity, only antipsychotic activity. Janssen then concludes that since Pireperone was not an antipsychotic and since the Patent Examiner did not care about dopamine activity, Janssen's withholding of Pirenperone's activity as a potent dopamine antagonist cannot be the basis for inequitable conduct.

As shown *infra (DFF152-DFF173),* Defendants have established that Pirenperone is an antipsychotic (by Janssen's own definition) and that the Examiner did care about a compound's dopamine activity. Accordingly, withholding of Pirenperone's activity as a potent dopamine antagonist was material.

Moreover, it is very telling that this defense against inequitable conduct (which is grounded upon the false premise that Pirenperone is not an antipsychotic) is of very recent origin. If the Court reviews Janssen's opposition to Mylan's

application to amend its Answer to plead inequitable conduct, the Court will find no trace of such an argument. *See* D.I. No. 56.

IX. CROSS-REFERENCE TO PLAINTIFFS' PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

A. REBUTTAL TO PLAINTIFFS' PRELIMINARY STATEMENT

JFF/CL ¶¶ *1-12*: Much of Janssen's preliminary statement relates to legal and factual irrelevancies, which Defendants need not address. With regard to relevant issues, Defendants do agree with Janssen that Defendants' obviousness case is not based upon Risperidone, but rather on Compound 11 (which appears in all of the claims of the '663 patent). Janssen also correctly asserts that Defendants argue that a prior art compound, Pirenperone, could be modified to create Compound 11 and that such a compound was therefore obvious, when the '663 patent was filed in March 1985. Beyond this, however, Janssen resorts to its litigation-induced theme that many compounds other than Pirenperone could have been selected for development purposes, and that Defendants made no effort, other than hindsight, to show why anyone of skill in the art would have focused upon Pirenperone. The allegation of a failure of proof is based on the standards Janssen alleges are set forth in *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharm., Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000). However, Janssen reads into *Yamanouchi* legal standards that simply do not exist, while at the same time ignoring binding Federal

Circuit precedent (even that cited in *Yamanouchi* itself), which provides the rules of decision relevant to this case.

With respect to the issue of inequitable conduct, Janssen correctly points out that Mylan did not introduce live testimony at trial directed to its inequitable conduct defense, other than that provided by Dr. Dellenbaugh. Janssen conveniently ignores the fact that Mylan's inequitable conduct defense indeed is supported through deposition testimony, as fully discussed in Defendant's opening Post-Trial Brief. In support, Janssen argues that because Dr. Wolff did not testify with respect to inequitable conduct, Mylan therefore abandoned its position. A curious position indeed, given that Janssen filed a motion *in limine* to exclude Dr. Wolff from testifying at all on the basis that Dr. Wolff should be precluded from "*marshalling the evidence* about inequitable conduct and offering testimony on *legal issues* and *intent.*" (emphasis original). At trial, Mylan chose to use its limited time with Dr. Wolff to focus upon the obviousness issues and spent considerable time in providing an overview of the chemistry and biochemistry necessary for the Court to place in context the issues to be decided in this case.

B. REBUTTAL TO JANSSEN'S FACTUAL BACKGROUND

JFF/CL ¶¶ 13-31: The background of schizophrenia is discussed, to which no response is necessary. Paragraphs 32 through 34 discuss the various attributes of Risperdal®, which contains Risperidone, not Compound 11 and, accordingly,

are not relevant to the present litigation. As indicated, Defendants are attacking the patentability of Compound 11, not Risperidone.

JFF/CL ¶¶ *35-39*: The factual background to the current litigation is discussed, but not without a high level of "spin." For example, *JFF/CL* ¶ *37* implies that Mylan amended its ANDA to include a Paragraph IV certification because a month earlier DRL had filed an Abbreviated New Drug Application ("ANDA") containing a Paragraph IV certification with respect to the '663 patent. Of course, as Janssen is well aware, DRL's action in filing with the FDA was not public, and there was no evidence that Mylan was aware of DRL's earlier filing (because no such evidence exists). As indicated in *JFF/CL* ¶¶ *40 and 41*, infringement has been stipulated, because all the claims of the '663 patent cover Risperidone, the active agent in Risperdal®, and no one can sell a generic product absent the active ingredient.

JFF/CL ¶¶ *42-46*: Various legal standards are addressed relating to the presumption of validity. In response, Defendants have set forth their own relevant authority in Paragraphs DCL8 to DCL9.

JFF/CL ¶¶ *49-55*: Janssen again repeats its allegations that Defendants' case is a failure, without record support, and with misapplication of the principles of obviousness set forth in Janssen's oft-cited case, *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharm., Inc.*, 231 F.3d 1339, 1343 (Fed. Cir. 2000). As to secondary considerations, there are none that relate to Compound 11, there is no

"embodiment of the claims" as existed in *Applied Materials*. There is no evidence that Compound 11 ever found its way out of the laboratory. *See DFF201-211.*

JFF/CL ¶¶ *58-81*: Legal argument concerning obviousness, and its application to the facts of the present case are presented, as viewed through the eyes of Janssen. Defendants strenuously disagree with both Janssen's position on the law and its application in this litigation. *See, Section II., supra.*

JFF/CL ¶¶ *82-110*: Janssen's desperate attempt to disparage Pirenperone as a logical starting point for developing an antipsychotic in the early 1980s. Janssen argues that Pirenperone was not an antipsychotic compound and, moreover, caused EPS in patients. Further, as Janssen's story goes, many compounds other than Pirenperone would have been more likely choices for developing an antipsychotic. According to Janssen, then, one skilled in the art would never have been motivated to choose Pirenperone for any purpose when developing an antipsychotic drug in the early 1980s. Defendants address such Janssen arguments in *Section V.A., supra.*

JFF/CL ¶¶ *154-219:* Janssen finally addresses the substance of Defendants' obviousness case. In those paragraphs, Janssen again attempts to argue against the clear and convincing trial record which establishes everything promised by Defendants in the opening statement. Pirenperone would have been a logical compound for modification in developing a better antipsychotic drug, and one starting with Pirenperone would have recognized that had a short half-life, that the

source of the short half-life ("the keto group") would have been apparent, that the means to "fix" the problem with the keto group was known in the prior art, and that there was a reasonable expectation that adopting such a modification would result in a compound with retained dopamine (antipsychotic) affect. Those paragraphs are addressed in Paragraphs DFF103 to DFF148 and Section IV., *supra.*

JFF/CL ¶¶ *220-273*: Janssen attempts to argue that Compound 11 somehow has the benefit of secondary considerations of nonobviousness. These paragraphs demonstrate how far Janssen is willing to stretch to save the '663 patent. That Compound 11 has no such secondary considerations in its favor is addressed in Paragraphs DFF201 to DFF215 and Section VI., *supra.*

JFF/CL ¶¶ *274-352*: address Mylan's inequitable conduct defense. Mylan's response thereto is set forth in Section VII., *supra.*

X. CONCLUSION

For the foregoing reasons, Defendants respectfully request that the Court find all claims of the '663 patent invalid as obvious, that the '663 patent is unenforceable due to inequitable conduct on the part of Janssen during the prosecution of the '663 patent, and award Defendants their attorneys' fees and other relief as set forth in their answers and counterclaims.

Respectfully submitted,

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Date: August 24, 2006

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